```
     FILE 'CAPLUS, WPIDS, MEDLINE, DRUGU, PHIC, PHIN, DRUGB, PHARMAML' ENTERED
     AT 14:13:21 ON 17 OCT 2003
L2        119693 S (LANTHANUM OR LA2CO3? OR FOSRENOL OR PHOSBLOC)
L3         77171 S (BONE OR DENTAL? OR PERIODONTAL? OR TEETH OR TOOTH) (5A) (FOR
L4        284256 S OSTEOPOROSIS OR PAGET? DISEASE OR OSTEOARTHRITIS OR ARTHRIT?
L5         70721 S MULTIPLE MYELOM? OR BONE TURNOVER# OR OSTEOLYTIC BONE DISEASE
L6         52913 S (BONE OR TEETH OR TOOTH OR PERIODONTAL) (5A) (GROW? OR GENERA
L7            25 S L2 (100A) (L3 OR L4 OR L5 OR L6)
L8            23 DUP REM L7 (2 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 14:26:46 ON 17 OCT 2003

     FILE 'CAPLUS, WPIDS, MEDLINE, DRUGU, PHIC, PHIN, DRUGB, PHARMAML' ENTERED
     AT 14:37:07 ON 17 OCT 2003
L9             8 S (BONE# (5A) (DISEASE# OR AILMENT# OR CONDITION# OR TREATMENT#
L10            4 S L9 NOT L8

=> d que l9; d que l10
L2        119693 SEA (LANTHANUM OR LA2CO3? OR FOSRENOL OR PHOSBLOC)
L9             8 SEA (BONE# (5A) (DISEASE# OR AILMENT# OR CONDITION# OR
                  TREATMENT# OR SUPPLEMENT?)) (100A) L2



L2        119693 SEA (LANTHANUM OR LA2CO3? OR FOSRENOL OR PHOSBLOC)
L3         77171 SEA (BONE OR DENTAL? OR PERIODONTAL? OR TEETH OR TOOTH) (5A)
                  (FORMATION# OR FRACTURE# OR TRAUMA? OR DEFICIT OR SURGERY OR
                  CHEMOTHERAP? OR RADIOTHERAP?)
L4        284256 SEA OSTEOPOROSIS OR PAGET? DISEASE OR OSTEOARTHRITIS OR
                  ARTHRIT? OR ACHONDROPLAS? OR OSTEOCHODRYTI? OR HYPERPARATHYROID
                  ? OR OSTEOGENESIS IMPERFECTA OR HYPOPHOPHATASIA OR FIBROMATOUS
                  LESION# OR FIBROUS DISPLASIA
L5         70721 SEA MULTIPLE MYELOM? OR BONE TURNOVER# OR OSTEOLYTIC BONE
                  DISEASE# OR OSTEOMALACI? OR PERIODONTAL DISEASE#
L6         52913 SEA (BONE OR TEETH OR TOOTH OR PERIODONTAL) (5A) (GROW? OR
                  GENERAT? OR REGENERAT? OR REPAIR? OR HEAL?)
L7            25 SEA L2 (100A) (L3 OR L4 OR L5 OR L6)
L8            23 DUP REM L7 (2 DUPLICATES REMOVED)
L9             8 SEA (BONE# (5A) (DISEASE# OR AILMENT# OR CONDITION# OR
                  TREATMENT# OR SUPPLEMENT?)) (100A) L2
L10            4 SEA L9 NOT L8


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L8 ANSWER 1 OF 23 PHIN COPYRIGHT 2003 PJB on STN

AN 2002:12060 PHIN
DN S00758568
DED 12 Jun 2002
TI Fosrenol shows 12-month bone benefits
SO Scrip (2002) No. 2754 p23
DT Newsletter
FS FULL
TX The results show that there was no progression to low **bone turnover** states during the 12 months in those patients treated with **Fosrenol**. Rates of adynamic bone disease for **Fosrenol** patients were 15% at baseline compared with 0% after 12 months. For calcium carbonate patients these figures were 13% and 10% respectively. The rates of **osteomalacia** for both **Fosrenol** and calcium carbonate patients were 3% at baseline compared with 0% after 12 months.

L8 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
AN 2002:10286 CAPLUS
DN 136:64161
TI Lanthanum compounds for the treatment of bone diseases
IN Atherton, Nigel Derek; Totten, Joseph Wilson; Gaitonde, Michael David
PA Shire Holdings AG, Switz.
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002000227	A2	20020103	WO 2001-GB2836	20010626
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002051822	A1	20020502	US 2001-891206	20010626
	EP 1294384	A2	20030326	EP 2001-940848	20010626
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	GB 2000-15745	A	20000627		
	WO 2001-GB2836	W	20010626		

AB The invention provides a method for enhancing **bone formation**, inhibiting osteoclastic differentiation, and/or activating osteoblastic differentiation whereby to manage, treat or achieve prophylaxis of bone disease which comprises administering to a human or animal subject suffering from, or susceptible to bone disease a therapeutically or prophylactically effective amt. of a **lanthanum** compd.
AB The invention provides a method for enhancing **bone formation**, inhibiting osteoclastic differentiation, and/or activating osteoblastic differentiation whereby to manage, treat or achieve prophylaxis of bone disease which comprises administering to a human or animal subject suffering from, or susceptible to bone disease a therapeutically or prophylactically effective amt. of a **lanthanum** compd.
IT Bone, disease
(**achondroplasia**; **lanthanum** compds. for treatment of

bone diseases)
IT Dwarfism
(**achondroplastic**; **lanthanum** compds. for treatment of bone diseases)
IT **Bone**
(**deficit** and remodeling disorder; **lanthanum** compds. for treatment of bone diseases)
IT Neoplasm
(fibroma, **fibromatous lesions**; **lanthanum** compds. for treatment of bone diseases)
IT **Bone**, disease
(**fracture**; **lanthanum** compds. for treatment of **bone** diseases)
IT Bone, disease
Bone formation
Cell differentiation
Chemotherapy
Drug delivery systems
Human
Hyperparathyroidism
Multiple myeloma
Osteoarthritis
Osteoclast
Osteomalacia
Periodontium, disease
Prosthetic materials and Prosthetics
Radiotherapy
Rheumatoid **arthritis**
Rickets
Surgery
(**lanthanum** compds. for treatment of **bone** diseases)
IT Bone, disease
(**osteogenesis imperfecta**; **lanthanum** compds. for treatment of bone diseases)
IT Menopause
(postmenopause, post-menopausal **osteoporosis**; **lanthanum** compds. for treatment of bone diseases)
IT Steroids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(steroid-induced **osteoporosis**; **lanthanum** compds. for treatment of bone diseases)
IT **Osteoporosis**
(therapeutic agents; **lanthanum** compds. for treatment of bone diseases)
IT Injury
(**trauma**, **bone**; **lanthanum** compds. for treatment of bone diseases)

L8 ANSWER 3 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-590413 [63] WPIDS
DNN N2002-468619 DNC C2002-166877
TI Determining the health status of a mammal comprises determining at least one erythrocyte sedimentation rate (ESR) of an anticoagulated sample of whole blood in the presence of an ESR-modulating agent e.g., epinephrine or collagen.
DC B04 D16 S03
IN KHALIL, M; SPILLERT, C R
PA (SPIL-I) SPILLERT C R; (KHAL-I) KHALIL M
CYC 95
PI WO 2002008728 A1 20020131 (200263)* EN 28p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ

LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002115222 A1 20020822 (200270)
AU 2001081359 A 20020205 (200281)
US 6514766 B2 20030204 (200313)
ADT WO 2002008728 A1 WO 2001-US41428 20010726; US 2002115222 A1 Provisional US 2000-221464P 20000726, US 2001-915198 20010725; AU 2001081359 A AU 2001-81359 20010726; US 6514766 B2 Provisional US 2000-221464P 20000726, US 2001-915198 20010725
FDT AU 2001081359 A Based on WO 2002008728
PRAI US 2001-915198 20010725; US 2000-221464P 20000726
AB WO 200208728 A UPAB: 20030101
NOVELTY - Determining the health status of a mammal comprises determining at least one erythrocyte sedimentation rate (ESR) of an anticoagulated sample of whole blood in the presence of an ESR-modulating agent.
USE - The method is useful in improving the diagnostic specificity of an ESR determination and in determining the health status of a mammal (claimed). Prognostic uses include determining whether a cardiac patient will be a candidate for an angioplastic procedure or more extensive surgery such as a bypass operation. The method can also be used to determine the likelihood or risk of acute or chronic coronary heart disease.
ADVANTAGE - The method provides an improved ESR test in terms of value, utility and sensitivity in the diagnosis, monitoring and prognostication of various diseases and conditions. Prior art ESR tests lack sensitivity in some disease states and are rarely elevated in asymptomatic individuals who may have occult disease.
Dwg.0/0
TECH. . .
or disease selected from the group comprising inflammation, sickle cell disease, osteomyelitis, stroke, myocardial infarction, cancer, pregnancy, infection, atherosclerosis, rheumatoid **arthritis**, ischemic heart disease, and trauma. The health status is also candidacy for coronary artery angioplasty. The ESR is performed on. . . Modulating Agent: The ESR-modulating agent is selected from the group comprising:
(1) a metal ion selected from silver, mercuric and **lanthanum** ions;
(2) a polymer selected from methylcellulose and polyvinylpyrrolidone;
(3) epinephrine;
(4) an oxidant, preferably hydrogen peroxide;
(5) a procoagulant agent, preferably Russell's viper. . .

L8 ANSWER 4 OF 23 MEDLINE on STN
AN 2003071380 MEDLINE
DN 22469329 PubMed ID: 12582469
TI Recent advances in nephrology: highlights from the 35th annual meeting of the American society of nephrology.
AU Cases Aleix
CS Nephrology Unit, Hospital Clinic, Barcelona, Spain.. acases@medicina.ub.es
SO Drugs Today (Barc), (2002 Dec) 38 (12) 797-805.
Journal code: 101160518. ISSN: 0025-7656.
CY Spain
DT Conference; Conference Article; (CONGRESSES)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20030214
Last Updated on STN: 20030521
Entered Medline: 20030520
AB The 35th Annual Meeting of the American Society of Nephrology, held in Philadelphia, Pennsylvania, United States (October 30 to November 4, 2002) presented the newest advances in basic and clinical nephrology science. Several presentations and symposia discussed the effects of various interventions and risk factors in clinical outcomes in dialysis patients.

The recent evidences of pure red cell aplasia secondary to neutralizing antibodies against erythropoietin were also extensively discussed in a special symposium. Recent advances in the management of calcium phosphorus metabolism and secondary **hyperparathyroidism**, such as the clinical efficacy and safety of AMG-073, a new calcimimetic agent in the control of **hyperparathyroidism** in chronic kidney disease patients, or the use of sevelamer or **lanthanum** carbonate as phosphate binders, were presented. The results in animal models on improved sparing of renal function with rapamycin versus cyclosporin A represent a promising advance in renal transplantation. Finally, the recent discoveries with the newly identified disease gene PKHD1, which causes autosomal recessive polycystic kidney disease, were also presented at the meeting.

AB . . . erythropoietin were also extensively discussed in a special symposium. Recent advances in the management of calcium phosphorus metabolism and secondary **hyperparathyroidism**, such as the clinical efficacy and safety of AMG-073, a new calcimimetic agent in the control of **hyperparathyroidism** in chronic kidney disease patients, or the use of sevelamer or **lanthanum** carbonate as phosphate binders, were presented. The results in animal models on improved sparing of renal function with rapamycin versus. . .

L8 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
AN 2002:356272 CAPLUS
DN 136:336374
TI The role of trace elements in uremic toxicity
AU Vanholder, Raymond; Cornelis, Rita; Dhondt, Annemieke; Lameire, Norbert
CS Department of Internal Medicine, Nephrology Division, University Hospital Gent, Ghent, B 9000, Belg.
SO Nephrology, Dialysis, Transplantation (2002), 17(Suppl. 2), 2-8
CODEN: NDTREA; ISSN: 0931-0509
PB Oxford University Press
DT Journal; General Review
LA English
AB A review. Although most research on uremic toxicity has focused on the retention or removal of org. solutes, subtle changes in the concn. of inorg. compds. are also of importance because these compds. may have significant clin. consequences. Potential clin. implications include increased risk of cancer, cardiovascular disease, immune deficiency, anemia, renal function impairment, and bone disease. In uremic patients, the most important factor affecting trace element concn. is the degree of renal failure and modality of renal replacement therapy. Accumulation of trace elements in hemodialysis patients has resulted from dialyzate contaminated with aluminum and strontium. Several trace elements have been implicated in the decline of renal function. These include arsenic, cadmium, copper, germanium, lead, and mercury. In uremic patients, aluminum, cadmium, chromium, lanthanum, strontium, and zinc have been shown to accumulate in bone. In addn. to substantial evidence linking aluminum to renal osteodystrophy, studies have also implicated cadmium, iron, and strontium in bone disease. Studies using a rat model of chronic renal failure have demonstrated an assocn. between **lanthanum** accumulation and mineralization defects characteristic of **osteomalacia**. Investigations of arsenic accumulation in animal models have demonstrated that speciation of trace elements potentially may alter toxicities of trace elements accumulated in uremic patients. Conversely, the presence of uremic toxins may also alter the uptake and toxicity of certain trace elements. Although research in uremic patients has focused primarily on the total concns. of trace elements, the evolution of both inorg. and org. species should be considered sep.
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A review. Although most research on uremic toxicity has focused on the retention or removal of org. solutes, subtle changes in the concn. of

inorg. compds. are also of importance because these compds. may have significant clin. consequences. Potential clin. implications include increased risk of cancer, cardiovascular disease, immune deficiency, anemia, renal function impairment, and bone disease. In uremic patients, the most important factor affecting trace element concn. is the degree of renal failure and modality of renal replacement therapy. Accumulation of trace elements in hemodialysis patients has resulted from dialyzate contaminated with aluminum and strontium. Several trace elements have been implicated in the decline of renal function. These include arsenic, cadmium, copper, germanium, lead, and mercury. In uremic patients, aluminum, cadmium, chromium, lanthanum, strontium, and zinc have been shown to accumulate in bone. In addn. to substantial evidence linking aluminum to renal osteodystrophy, studies have also implicated cadmium, iron, and strontium in bone disease. Studies using a rat model of chronic renal failure have demonstrated an assocn. between **lanthanum** accumulation and mineralization defects characteristic of **osteomalacia**. Investigations of arsenic accumulation in animal models have demonstrated that speciation of trace elements potentially may alter toxicities of trace elements accumulated in uremic patients. Conversely, the presence of uremic toxins may also alter the uptake and toxicity of certain trace elements. Although research in uremic patients has focused primarily on the total concns. of trace elements, the evolution of both inorg. and org. species should be considered sep.

L8 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:536728 CAPLUS
DN 136:156374
TI Biological glass coating on ceramic materials: in vitro evaluation using primary osteoblast cultures from healthy and osteopenic rat bone
AU Torricelli, P.; Verne, E.; Brovarone, C. V.; Appendino, P.; Rustichelli, F.; Krajewski, A.; Ravaglioli, A.; Pierini, G.; Fini, M.; Giavaresi, G.; Giardino, R.
CS Experimental Surgery Department, Research Institute Codivilla-Putti IOR, Bologna, Italy
SO Biomaterials (2001), 22(18), 2535-2543
CODEN: BIMADU; ISSN: 0142-9612
PB Elsevier Science Ltd.
DT Journal
LA English
AB ZrO2 and Al2O3 substrates were successfully coated by a double layer of a silica-based glass named RKKP, using a low-cost firing technique. RKKP is a glass well known for its bioactivity; therefore, a RKKP coating on Al2O3 or ZrO2, allows to combine the excellent mech. properties of these strong ceramic substrates with its bioactivity. ZrO2 samples were easily coated using a double layer of RKKP by a simple enameling technique. To accommodate the thermal expansion coeff. mismatch between Al2O3 and RKKP, this substrate was coated using a multilayered composite approach. All of the coatings were characterized from a morphol. and compositional point of view, and an extensive biol. evaluation was performed using fresh rat osteoblasts. Osteoblast primary cultures were derived from the trabecular bone of femoral condyles harvested from intact (NB) and osteopenic (OB) rats. After characterization of their phenotype, osteoblasts were seeded on material samples of ZrO2 or Al2O3 coated with RKKP, and cultured for 7 days. Cell proliferation (MTT test) and cell differentiation (alk. phosphatase activity) were evaluated at the end of the expt., to assess osteoblast behavior in the presence of biomaterials and det. if the results were related to the host bone quality. Results of both materials showed a good level of biocompatibility. In particular, MTT significant higher values were detected in NB cultures on ZrO2-RKKP samples; ALP activity significantly increased in NB cultures on Al2O3-RKKP and in OB cultures on both coated samples.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT Fluoride glasses

Phosphosilicate glasses
RL: BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**lanthanum**- and potassium-doped calcium magnesium sodium fluoride tantalophosphosilicate; biol. glass coating on ceramic materials: in vitro evaluation using primary osteoblast cultures from **healthy** and osteopenic rat **bone**)

IT 1312-81-8, **Lanthanum** oxide 12136-45-7, Potassium oxide, biological studies
RL: BSU (Biological study, unclassified); DEV (Device component use); MOA (Modifier or additive use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RKKP glass contg.; biol. glass coating on ceramic materials: in vitro evaluation using primary osteoblast cultures from **healthy** and osteopenic rat **bone**)

L8 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:455673 CAPLUS
DN 129:80149
TI Determination of elements in bone of tuberculous-arthritis patients by radioisotope x-ray fluorescence analysis
AU Akyuz, T.; Bassari, A.; Akyuz, S.
CS Cekmece Nuclear Research Training Center, Istanbul, Turk.
SO Journal of Radioanalytical and Nuclear Chemistry (1998), 232(1-2), 253-255
CODEN: JRNCDM; ISSN: 0236-5731
PB Elsevier Science S.A.
DT Journal
LA English
AB Ca, P, Zn, Sr, Ba, La and Ce in human femoral bone of tuberculosis-arthritis (Koch-arthritis) were detd. by radioisotope energy dispersive x-ray fluorescence (EDXRF). P, Ca, and Sr in the control were higher than those in the tuberculosis-arthritis group, while the concns. of Zn, Ba, La, and Ce are not different.
ST tuberculosis arthritis bone mineral; Koch arthritis bone mineral; calcium phosphorus zinc tuberculosis arthritis bone; strontium barium tuberculosis arthritis bone; **lanthanum** cerium tuberculosis **arthritis** bone
IT 7439-91-0, **Lanthanum**, biological studies 7440-24-6, Strontium, biological studies 7440-39-3, Barium, biological studies 7440-45-1, Cerium, biological studies 7440-66-6, Zinc, biological studies 7440-70-2, Calcium, biological studies 7723-14-0, Phosphorus, biological studies
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(minerals in bone of tuberculous-**arthritis** patients detd. by radioisotope x-ray fluorescence anal.)

L8 ANSWER 8 OF 23 PHIN COPYRIGHT 2003 PJB on STN

AN 97:6818 PHIN
DN S00532228
DED 11 Apr 1997
TI Shire plans new acquisitions
SO Scrip (1997) No. 2222 p9
DT Newsletter
FS FULL
TX The . . . its recent acquisition of Pharmavene. It plans to market (or co-promote) to specialists compounds from its development pipeline, including Lambda (**lanthanum** salt) for phosphate binding in kidney disease, Sigma for **osteoporosis**, and a controlled-release selegiline for Parkinson's disease.

L8 ANSWER 9 OF 23 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN

AN 1995-21659 DRUGU G
TI Phonophoresis - is it a reality
AU Meidan V M; Walmsley A D; Irwin W J
CS Univ.Aston; Univ.Birmingham
LO Birmingham, U.K.
SO Int.J.Pharm. (118, No. 2, 129-49, 1995) 2 Fig. 2 Tab. 102 Ref.
CODEN: IJPHDE ISSN: 0378-5173
AV Pharmaceutical Sciences Institute, Aston University, Aston Triangle, Birmingham B4 7ET, England.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Phonophoresis, the application of ultrasound to enhance percutaneous drug delivery, is reviewed, with reference to proposed mechanisms, and its study in-vitro, in animals and in human volunteer trials. Drugs studied phonophoretically have included ibuprofen, indomethacin (IN), digoxin, mannitol, lanthanum hydroxide, inulin, hydrocortisone, physostigmine, salicylic acid, insulin, amphotericin B, benzocaine, benzethonium Cl, benzydamine HCl, dibucaine, ethyl nicotinate, fluocinolone acetonide, hexyl nicotinate, methyl nicotinate, lignocaine (LC), prilocaine, Na pertechnetate and Na diethylenetriamine pentaacetic acid. It is concluded that phonophoresis is possible for certain molecules under certain conditions, and that ultrasonic heating is its main mechanism, but its therapeutic value is still under question.
ABEX. . . or dogs, mannitol, inulin (with shortened lag time for both), insulin or IN in rats, physostigmine in rats and guinea-pigs, **lanthanum** hydroxide or 14C-salicylic acid in hairless guinea-pigs (the latter with reduced lag time), and amphotericin B (but not IN) in. . . frequency, and has been improved by combination with DMSO. Phonophoresis has enhanced delivery of hydrocortisone in a study of 102 **arthritic** patients, and of fluocinolone acetonide, LC + prilocaine (at 2 W/sq.cm + 0.87 MHz for 5 min, but not LC. . .

L8 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:404155 CAPLUS
DN 121:4155
TI Radiolabeled compositions containing a calcific matrix and their use for treatment of rheumatoid arthritis
IN McMillan, Kenneth; Simon, Jaime
PA Dow Chemical Co., USA
SO U.S., 7 pp. Cont.-in-part of U.S. 5,137,709.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5300281	A	19940405	US 1992-906998	19920701
	US 5137709	A	19920811	US 1991-656397	19910215
PRAI	US 1991-656397	A2	19910215		

AB Radioactive compns. contg. a calcific matrix and methods for using the compns. for therapeutic radiation treatment including rheumatoid arthritis are disclosed. A layered mixed metal hydroxide (LMMH) was prepd. from MgCl2, AlCl3, and NH4OH. The LMMH was added to a hydroxylapatite/153Sm mixt. and the mixt. was allowed to sit for 10 min before injection into the synovium of a rabbit. No leakage of radioactivity from the synovium was obsd.
IT 10098-91-6, Yttrium-90, biological studies 13967-65-2, Holmium-166, biological studies 13981-28-7, **Lanthanum**-140, biological studies 14041-42-0, Gadolinium-159, biological studies 14041-44-2, Ytterbium-175, biological studies 14265-75-9, Lutetium-177, biological studies 14378-26-8, Rhenium-188, biological studies 14391-96-9, Scandium-47, biological studies 14998-63-1, Rhenium-186, biological

studies 15766-00-4, Samarium-153, biological studies
RL: BIOL (Biological study)
(calcific matrix with sorbed, for radiation ablation treatment of rheumatoid **arthritis**)

L8 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1991:520085 CAPLUS
DN 115:120085
TI Radiolabeled iron hydroxide colloid compositions, their use and process for their preparation
IN Simon, Jaime; Cooper, Lance A.; McMillan, Kenneth; Wilson, David A.
PA Dow Chemical Co., USA
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9109622	A1	19910711	WO 1990-US7522	19901218
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	US 5061476	A	19911029	US 1989-458049	19891227
	CA 2046308	AA	19910628	CA 1990-2046308	19901218
	CA 2046308	C	20001128		
	EP 460205	A1	19911211	EP 1991-903521	19901218
	EP 460205	B1	20020424		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 04505023	T2	19920903	JP 1991-503520	19901218
	JP 3155273	B2	20010409		
	AT 216596	E	20020515	AT 1991-903521	19901218
PRAI	US 1989-458049	A	19891227		
	WO 1990-US7522	W	19901218		

AB Radiolabeled colloid compns. for the treatment of arthritis comprise spherical aggregation of radioactive metal in iron hydroxide particles. The compns. are prepd. (1) by prepg. an iron hydroxide colloid by pptg. an iron soln. with an alkali metal hydroxide and (2) sorbing onto the colloid a radionuclide of Sm-153, Ho-166, In-115m, Y-90, Gd-159, La-140, Lu-177, or Yb-175. The compn. at 500-150,000 rads is administered to the synovium of a joint. The colloids prepd. by the sorption process remain in the synovium better than similar entrapped radionuclide formulations prepd. by the copptn. process. To 0.3 mL of Fe(OH)2 colloid prepd. by treating FeSO4 soln. with NaOH soln. was added 30 .mu.L of Sm-153 soln. in 0.1 HCl with stirring to give a colloid, which was injected (100 .mu.L) into the synovium of stifle of the hind leg in a rabbit; greater than 99% of the injected dose of radioactivity remained in the synovium with no leakage into surrounding tissues during 4 h period.
IT 10098-91-6, Yttrium-90, biological studies 13967-65-2, Holmium-166, biological studies 13981-28-7, **Lanthanum**-140, biological studies 14041-42-0, Gadolinium-159, biological studies 14041-44-2, Ytterbium-175, biological studies 14265-75-9, Lutetium-177, biological studies 15766-00-4, Samarium-153, biological studies
RL: BIOL (Biological study)
(aggregation of, on iron hydroxide colloids, for synovectomy in **arthritis** treatment)

L8 ANSWER 12 OF 23 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1990-11316 DRUGU P
TI Suppression of Mitogen- and Antigen-Induced Lymphocyte Proliferation by Lanthanides.
AU Yamage M; Evans C H
LO Bern, Switzerland; Pittsburgh, Pennsylvania, United States
SO Experientia (45, No. 11-12, 1129-31, 1989) 4 Fig. 33 Ref.
CODEN: EXPEAM ISSN: 0014-4754

AV Research Laboratory for Biomaterials, Inselspital, University of Bern, CH-3010 Bern, Switzerland.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB **Lanthanum** (La3+), samarium (Sm3+), erbium (Er3+) and lutetium (Lu3+) inhibited the proliferatie response of human lymphocytes to con A, pokeweed mitogen (PWM), phytohemagglutinin (PHA) and the 'purified protein derivative' (PPD) of the tuberculin in descending order of potency. It is speculated that lanthanides (Ln3+) might find therapeutic use in **arthritis**.
AB **Lanthanum** (La3+), samarium (Sm3+), erbium (Er3+) and lutetium (Lu3+) inhibited the proliferatie response of human lymphocytes to con A, pokeweed mitogen. . . (PPD) of the tuberculin in descending order of potency. It is speculated that lanthanides (Ln3+) might find therapeutic use in **arthritis**.

L8 ANSWER 13 OF 23 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1987-06492 DRUGU P C
TI Studies on Anti-Inflammatory Activity of some Lanthanon Complexes of Bioactive Organic Molecules.
AU Singh L; Mohan G; Parashar R K; Tripathi S P; Sharma R C
LO Agra, India
SO Curr.Sci. (55, No. 17, 846-48, 1986) 2 Fig. 1 Tab. 12 Ref.
CODEN: CUSCAM ISSN: 0011-3891
AV Chemical Laboratories, Agra University, Agra 282 004, India.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AB **Lanthanum** (La), praseodymium (Pr), neodymium (Nd), gadolinium (Gd) and dysprosium (Dy) complexes of pyridine- 2,6-dicarboxylate (PDA), 8-hydroxy-quinoline (HQ) and 2-picolinic acid (PIC) were prepared and antiinflammatory activity was tested in rats with carragheenin paw edema, cotton pellet granuloma and formaldehyde induced **arthritis**. Only La(III)-PDA-HQ showed some activity in subacute and chronic inflammation. Oxyphenbutazone was used for comparison.
AB **Lanthanum** (La), praseodymium (Pr), neodymium (Nd), gadolinium (Gd) and dysprosium (Dy) complexes of pyridine- 2,6-dicarboxylate (PDA), 8-hydroxy-quinoline (HQ) and 2-picolinic acid. . . (PIC) were prepared and antiinflammatory activity was tested in rats with carragheenin paw edema, cotton pellet granuloma and formaldehyde induced **arthritis** . Only La(III)-PDA-HQ showed some activity in subacute and chronic inflammation. Oxyphenbutazone was used for comparison.

L8 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1987:12177 CAPLUS
DN 106:12177
TI Determination of trace amounts of lanthanum in animal tissues, especially in teeth and bones
AU Ishiguro, Yoshio; Goto, Kazuo; Kobayashi, Yasuko; Nakashima, Ryozo; Shibata, Shozo
CS Gov. Ind. Res. Inst., Nagoya, 462, Japan
SO Nagoya Kogyo Gijutsu Shikensho Hokoku (1986), 35(3), 97-101
CODEN: NKGSAR; ISSN: 0027-7614
DT Journal
LA Japanese
AB Following the topical application of a La-contg. soln. to rat teeth, La was detd. in teeth and bones by emission spectroscopy (ES) after digestion of the biol. sample with a HNO3-perchloric acid mixt. La was pptd. as lanthanum oxalate [537-03-1] together with Ca oxalate from these 2 biol. samples. La oxalate was extd. with TTA (4,4,4-trifluoro-1-(2-thienyl)-1,3-butanedione into 4-methyl-2-pentanone, back-extd. into HNO3 (1M) and then

detd. by ES.
IT 537-03-1, **Lanthanum** oxalate
RL: FORM (Formation, nonpreparative)
(**formation** of, in **teeth** and **bone**, after topical application of **lanthanum** to teeth.)

L8 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1983:533635 CAPLUS
DN 99:133635
TI Effect of chlorhexidine and lanthanum on plaque formation
AU Waaler, Sonni Mette; Roella, Gunnar
CS Fac. Dent., Univ. Oslo, Oslo, Norway
SO Scandinavian Journal of Dental Research (1983), 91(4), 260-2
CODEN: SJDRAN; ISSN: 0029-845X
DT Journal
LA English
AB The effect of La2+ ions on the plaque formation inhibitory actions of chlorhexidine (I) [55-56-1] was investigated in healthy subjects. La2+ appears to be able to block some receptor sites for I and also to displace I which has already been adsorbed. Rinses with aq. solns. of La2+ reduced the clin. effect of I regardless of whether it was applied before or after the I mouthrinses. Since La2+ has an extremely high affinity for phosphate groups and these groups are reportedly abundent in plaque, it is suggested that phosphate groups are involved in the binding of I to receptor sites in the oral cavity.
IT **Tooth**
(plaque, **formation** of, chlorhexidine inhibition of, in humans, **lanthanum** effect on)

L8 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1982:607858 CAPLUS
DN 97:207858
TI Relative changes of the oral microflora in the induction and the lanthanum inhibition of dental caries in rats
AU Ozeki, Masami
CS Sch. Dent., Aichi-Gakuin Univ., Nagoya, Japan
SO Aichi Gakuin Daigaku Shigakkaishi (1982), 19(4), 364-98
CODEN: AGDSAB; ISSN: 0044-6912
DT Journal
LA Japanese
AB In rats infected with Streptoccus mutans, 20 mg of moist materials taken from the oral cavity with a cotton swab contained 106 colony-forming units. About 95% of the microflora isolated were identified, streptococci and gram-neg. bacilli being predominant. Infection with S. mutans decreased the population of S. equinus and Pasteurella pneumotropica, and increased caries formation. Administration of solns. contg. >4% La decreased the caries formation and the S. mutans population, although administration of lower La doses (<2%) did not change the S. mutans population appreciably. The adsorption of S. mutans on extd. teeth in the presence of sucrose in vitro was inhibited by La, suggesting that the decrease of caries formation by La is partially attributable to the inhibition of the adsorption of S. mutans on the teeth.
IT Mouth
(microorganisms of, **dental** caries **formation** response to **lanthanum** in relation to)
IT Microorganism
(of mouth, **dental** caries **formation** response to **lanthanum** in relation to)

L8 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1983:569039 CAPLUS
DN 99:169039
TI Distribution and fate of lanthanum in the tissues of rats administered lanthanum salt solutions - by means of swabbing the solutions on the teeth

and through stomach tube
AU Sakurai, Yasuo
CS Sch. Dent., Aichi-Gakuin Univ., Nagoya, Japan
SO Aichi Gakuin Daigaku Shigakkaishi (1982), 20(1), 1-19, 3 plates
CODEN: AGDSAB; ISSN: 0044-6912
DT Journal
LA Japanese
AB In rats, the treatment of teeth with a La3+ soln. caused replacement of Ca2+ in the enamel by La3+. Those teeth contained LaPO4, LaP5O14, and LaHP2O7 when >4% La salt soln.s were applied. However, the concn. of La in the enamel decreased rapidly for a month and then decreased slowly thereafter. The daily application of La3+ solns. increased the La3+ content in the liver, spleen, and femur, and produced the max. content in 1-2 mo. In the femur, most of La3+ was incorporated into the medulla. Although La3+ was accumulated in the liver, no significant toxic effects were obsd. In rats receiving La3+ directly into the stomach, the La3+ levels in the liver, spleen, and femur at the 14th day were less than those obsd. at the 7th day. However, La3+ was continuously accumulated in the kidney.
IT 12501-21-2 13778-59-1 13814-33-0
RL: FORM (Formation, nonpreparative)
(**formation** of, in **teeth** after **lanthanum** nitrate administration)

L8 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1981:597131 CAPLUS
DN 95:197131
TI Absorption of lanthanum by the enamel surface of rat teeth
AU Kobayashi, Yasuko; Ozeki, Masami; Yagi, Toshiharu; Hosoi, Tatsuoki; Yoshizaki, Nobuya; Sakurai, Yasuo
CS Sch. Dent., Aichi-Gakuin Univ., Nagoya, 464, Japan
SO Shika Kiso Igakkai Zasshi (1981), 23(2), 253-61
CODEN: SHKKAN; ISSN: 0385-0137
DT Journal
LA Japanese
AB La(NO3)3 soln. (8%) applied to teeth of rats once a day for 2 wk prevented caries formation, displaced Ca2+ in the enamel surface by La3+, and formed LaPO4, La4(P2O7)3, LaP5O14, and LaHP2O7.3H2O. La(NO3)3 prevented the adhesion of Streptococcus mutans to the teeth and inhibited the multiplication and growth of lactobacilli. About 15% of the La3+ dose applied was detected on the enamel surface 1, 2, and 3 mo after application, but no La3+ was detected after 5 mo.
IT 12501-21-2 13778-59-1 13814-33-0 13955-20-9
RL: FORM (Formation, nonpreparative)
(**formation** of, on **tooth** enamel after **lanthanum** nitrate application)

L8 ANSWER 19 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1979-88237B [49] WPIDS
TI Ceramic part for filling deficient bone - comprising porous ceramic moulding based on alumina and apatite.
DC L02 P32 P34
PA (KYOC) KYOTO CERAMIC CO LTD
CYC 1
PI JP 54138006 A 19791026 (197949)*
JP 61009075 B 19860319 (198615)
PRAI JP 1978-46804 19780419
AB JP 54138006 A UPAB: 19930901
A ceramic part, intended for use in the field of surgical operation in plastic surgery, etc., with a purpose of filling the **deficit** of **bone** after cutting operating is new. Part is a porous ceramic moulding having a large number of fine pores permitting the prolific penetration of bone, an outer shape without acute-angled corners, and a shortest outside dia. of >0.5 mm. Ceramic is composed of alumina and

apatite, together with an appropriate amt. of a substance impervious to X-rays, e.g., yttrium oxide, zirconium oxide, **lanthanum** oxide, etc..

Prod. can be used for filling small deficiencies of bone and even where the deficient portion of bone is large, it can be effected without causing damage to patient, and also greatly relieves pain. Prod. also is able to accelerate the prolific penetration of bone.

AB . . .
part, intended for use in the field of surgical operation in plastic surgery, etc., with a purpose of filling the **deficit** of **bone** after cutting operating is new. Part is a porous ceramic moulding having a large number of fine pores permitting the. . . of alumina and apatite, together with an appropriate amt. of a substance impervious to X-rays, e.g., yttrium oxide, zirconium oxide, **lanthanum** oxide, etc..

Prod. can be used for filling small deficiencies of bone and even where the deficient portion of. . .

L8 ANSWER 20 OF 23 MEDLINE on STN
AN 80075075 MEDLINE
DN 80075075 PubMed ID: 513186
TI Cellular relationship in the rat **bone** marrow studied by freeze **fracture** and **lanthanum** impregnation thin-sectioning electron microscopy.
AU Shaklai M; Tavassoli M
SO JOURNAL OF ULTRASTRUCTURE RESEARCH, (1979 Dec) 69 (3) 343-61. Journal code: 0376344. ISSN: 0022-5320.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198002
ED Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19800215
TI Cellular relationship in the rat **bone** marrow studied by freeze **fracture** and **lanthanum** impregnation thin-sectioning electron microscopy.

L8 ANSWER 21 OF 23 MEDLINE on STN
AN 80065401 MEDLINE
DN 80065401 PubMed ID: 508632
TI Junctional structures in haemopoiesis: a study of **bone** marrow using freeze-**fracture** and **lanthanum** impregnation techniques.
AU Tavassoli M; Shaklai M
SO BRITISH JOURNAL OF HAEMATOLOGY, (1979 Oct) 43 (2) 235-41. Journal code: 0372544. ISSN: 0007-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198002
ED Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19800228
AB Intercellular regions of contact in the haemopoietic compartment of normal rat **bone** marrow were studied using freeze-**fracture** and **lanthanum** tracer techniques. Small adhering junctions (like desmosomes and their variants) were found between haemopoietic and stromal cells but tight, gap or septate junctions could not be identified. These findings are in agreement with the concept that extensive junctional structures may be inconsistent with orderly development of this transient cell system, preventing the delivery of mature cells into the circulation

and resulting in ineffective haemopoiesis. Occasionally 'pinching off' of a portion of the cytoplasm of erythroid cells by stromal cells was seen, providing a means for intercellular communication. Structures similar to intercellular bridges responsible for direct intercellular communication were also seen.

TI Junctional structures in haemopoiesis: a study of **bone** marrow using freeze-**fracture** and **lanthanum** impregnation techniques.

AB Intercellular regions of contact in the haemopoietic compartment of normal rat **bone** marrow were studied using freeze-**fracture** and **lanthanum** tracer techniques. Small adhering junctions (like desmosomes and their variants) were found between haemopoietic and stromal cells but tight, gap. . .

L8 ANSWER 22 OF 23 PHARMAML COPYRIGHT 2003 MARKETLETTER on STN
AN 1668612 PHARMAML
TI Shire's Fosrenol is approvable, says FDA
SO Pharma Marketletter March 10, 2003
DT Newsletter
WC 430
TX . . . HCl] is another treatment option gaining ground) which have been shown to have the potential to cause the bone disease **osteomalacia**. One suggestion is that Shire is being asked to provide more information on the safety of **Fosrenol** with regards to bone, a task which is made the harder because hyperphosphatemia itself is associated with the bone disease renal osteodystrophy. The UK firm has already completed one study supporting the safety of **Fosrenol** on bone (Marketletter June 17, 2002).

L8 ANSWER 23 OF 23 PHARMAML COPYRIGHT 2003 MARKETLETTER on STN
AN 1663684 PHARMAML
TI Shire's Fosrenol clears bone safety hurdle
SO Marketletter June 17, 2002
DT Newsletter
WC 417
TX **Fosrenol** was compared in the study to a reference treatment (calcium carbonate). At baseline, 3% of the **Fosrenol** and calcium carbonate groups exhibited signs of **osteomalacia**, but no evidence of this was found at the end of the study. 15% of **Fosrenol** patients had signs of adynamic bone disease at the outset, compared to 13% of the comparator group. However, while this had disappeared in the **Fosrenol** group by study-end, it was still evident in 10% of the control group.
There was no evidence of low **bone turnover** status in patients treated with **Fosrenol**, although this is encountered in patients receiving standard therapy with calcium carbonate/aluminum hydroxide, said Shire, which also pointed to earlier. . .

L10 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:478053 CAPLUS
DN 139:173761
TI A multicenter study on the effects of **lanthanum** carbonate (**Fosrenol**) and calcium carbonate on renal **bone disease** in dialysis patients
AU D'Haese, Patrick C.; Spasovski, Goce B.; Sikole, Aleksander; Hutchison, Alastair; Freemont, Tony J.; Sulkova, Sylvie; Swanepoel, Charles; Pejanovic, Svetlana; Djukanovic, Llubica; Balducci, Alessandro; Coen, Giorgio; Sulowicz, Waldysaw; Ferreira, Anibal; Torres, Armando; Curic, Slobodan; Popovic, Milan; Dimkovic, Nada; De Broe, Marc E.
CS Department of Nephrology-Hypertension, University of Antwerp, Antwerp, Belg.
SO Kidney International, Supplement (2003), 85, S73-S78
CODEN: KISUDF; ISSN: 0098-6577
PB Blackwell Science, Inc.
DT Journal
LA English
AB Lanthanum carbonate (LC) (Fosrenol) is a novel new treatment for hyperphosphatemia. This phase III, open-label study compared the effects of LC and calcium carbonate (CC) on the course of renal osteodystrophy (ROD) in dialysis patients. LC was well tolerated and serum phosphate concns. were well controlled in both treatment groups. The incidence of hypercalcemia was lower in the LC group (6% vs. 49% for CC). Before treatment, subtypes of ROD were similarly distributed in both groups, with mixed ROD being most common. At 1-yr follow-up in the LC group, 5 of 7 patients with basal low bone turnover (either adynamic bone or osteomalacia) and 4 of 5 patients with basal hyperparathyroidism had evolved toward a normalization of their bone turnover. Only one LC-treated patient evolved toward adynamic bone compared with 6 patients in the CC group. In the LC group, the no. of patients having either adynamic bone, osteomalacia, or hyperparathyroidism decreased overall from 12 (36%) before treatment to 6 (18%), while in the CC group, the no. of patients with these types of ROD increased from 13 (43%) to 16 (53%). LC is a poorly absorbed, well-tolerated, and efficient phosphate binder. LC-treated dialysis patients show almost no development toward low bone turnover over 1 yr (unlike CC-treated patients), nor do they experience any aluminum-like effects on bone.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI A multicenter study on the effects of **lanthanum** carbonate (**Fosrenol**) and calcium carbonate on renal **bone disease** in dialysis patients
ST **lanthanum** carbonate calcium carbonate kidney **bone disease** hemodialysis; renal osteodystrophy hemodialysis Fosrenol
IT Dialysis
(hemodialysis; **lanthanum** carbonate (**Fosrenol**) vs. calcium carbonate effects on renal **bone disease** in dialysis patients)
IT Human
(**lanthanum** carbonate (**Fosrenol**) vs. calcium carbonate effects on renal **bone disease** in dialysis patients)
IT **Bone, disease**
(renal osteodystrophy; **lanthanum** carbonate (**Fosrenol**) vs. calcium carbonate effects on renal **bone disease** in dialysis patients)
IT 471-34-1, Calcium carbonate, biological studies 587-26-8, **Fosrenol** 7439-91-0D, **Lanthanum**, salts
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**lanthanum** carbonate (**Fosrenol**) vs. calcium carbonate effects on renal **bone disease** in dialysis

patients)
IT 14265-44-2, Phosphate, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolic disorder, hyperphosphatemia; **lanthanum** carbonate (**Fosrenol**) vs. calcium carbonate effects on renal **bone disease** in dialysis patients in relation to management of)

L10 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:291528 CAPLUS
DN 130:323894
TI Trace elements in human bone determined by neutron activation analysis
AU Aras, N. K.; Yilmaz, G.; Alkan, S.; Korkusuz, F.
CS Department Chemistry, Middle East Technical Univ., Ankara, Turk.
SO Journal of Radioanalytical and Nuclear Chemistry (1999), 239(1), 79-86
CODEN: JRNCDM; ISSN: 0236-5731
PB Elsevier Science B.V.
DT Journal
LA English
AB There is an evidence that some of the essential trace elements are crucial determinants of bone health. Excess or deficiency of these elements has a role in the development of bone diseases, therefore research on trace elements in bone is very important. Iliac crest bone biopsies were optioned from 12 persons undergoing orthopedic surgery due to any reason other than osteoporosis. Cortical and trabecular parts were sepd., and blood and fats were removed. Up to 30 minor and trace elements were detd. in these samples by INAA and other techniques and their relations were discussed.
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT 7439-89-6, Iron, biological studies 7439-91-0, **Lanthanum**, biological studies 7439-94-3, Lutetium, biological studies 7439-97-6, Mercury, biological studies 7439-98-7, Molybdenum, biological studies 7440-00-8, Neodymium, biological studies 7440-09-7, Potassium, biological studies 7440-17-7, Rubidium, biological studies 7440-19-9, Samarium, biological studies 7440-20-2, Scandium, biological studies 7440-23-5, Sodium, biological studies 7440-24-6, Strontium, biological studies 7440-25-7, Tantalum, biological studies 7440-29-1, Thorium, biological studies 7440-36-0, Antimony, biological studies 7440-38-2, Arsenic, biological studies 7440-39-3, Barium, biological studies 7440-43-9, Cadmium, biological studies 7440-45-1, Cerium, biological studies 7440-46-2, Cesium, biological studies 7440-47-3, Chromium, biological studies 7440-48-4, Cobalt, biological studies 7440-53-1, Europium, biological studies 7440-61-1, Uranium, biological studies 7440-66-6, Zinc, biological studies 7440-67-7, Zirconium, biological studies 7440-70-2, Calcium, biological studies 7726-95-6, Bromine, biological studies 7782-41-4, Fluorine, biological studies 7782-49-2, Selenium, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(in human **bones** in relation to **bone diseases**)

L10 ANSWER 3 OF 4 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-147852 [19] WPIDS
DNC C2002-045891
TI Use of **lanthanum** (III) compounds for enhancing bone formation, inhibiting osteoclastic differentiation and/or activating osteoblastic differentiation to treat **bone disease** such as osteoporosis.
DC B06
IN ATHERTON, N D; GAITONDE, M D; TOTTEN, J W
PA (SHIR-N) SHIRE HOLDINGS AG
CYC 97
PI WO 2002000227 A2 20020103 (200219)* EN 60p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

US 2002051822 A1 20020502 (200234)
AU 2001074341 A 20020108 (200235)
EP 1294384 A2 20030326 (200323) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR

ADT WO 2002000227 A2 WO 2001-GB2836 20010626; US 2002051822 A1 US 2001-891206 20010626; AU 2001074341 A AU 2001-74341 20010626; EP 1294384 A2 EP 2001-940848 20010626, WO 2001-GB2836 20010626

FDT AU 2001074341 A Based on WO 2002000227; EP 1294384 A2 Based on WO 2002000227

PRAI GB 2000-15745 20000627

AB WO 200200227 A UPAB: 20020321

NOVELTY - Enhancing bone formation, inhibiting osteoclastic differentiation and/or activating osteoblastic differentiation to manage, treat or achieve prophylaxis of **bone disease** comprises administering a **lanthanum** compound (preferably **lanthanum** (III)) to a human or animal.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a composition for the **treatment** of a **bone** remodeling disorder comprising the **lanthanum** (III) compound and a bone enhancing agent.

ACTIVITY - Osteopathic; Cytostatic; Antiarthritic; Antirheumatic; Antiinflammatory.

MECHANISM OF ACTION - Osteoblast differentiation stimulator; Osteoclast differentiation inhibitor. 8-10 week old mice were killed and tibia and femora were dissected free from adhering soft tissues. The bone ends were cut off and the marrow was flushed with alpha -minimal essential medium (alpha -MEM) supplemented with penicillin (100 IU/ml) and streptomycin (100 micro g/ml). Cells were centrifuged for 10 minutes and the cell pellet was resuspended in alpha -MEM containing 10% fetal calf serum. Cells were then incubated for 2 hours at 370 deg. C.

Nonadherent cells were duly removed and the attached bone marrow cells were cultured (1 multiply 106 cells/well = 1 ml) for 6 days.

Half of the media were changed at day 3 and the treatments replaced. At the end of the culture, the plates were fixed with 2% paraformaldehyde in PBS for 20 minutes.

To study the effect of the lanthanum (III) ion on Osteoclast differentiation, the following groups were included:

(A) baseline (including vehicle);

(B) control (baseline without 1,25-dihydroxyvitamin D3);

(C) baseline + 100/500/1000/5000/15000 ng/ml lanthanum.

Six replicates were included in each group and the test was performed twice.

Osteoclast formation was determined by measuring tartrate-resistant acid phosphate (TRAP) activity from the culture media.

Combined results of relative TRAP 5b activities in three osteoclast differentiation assay were as follows: Osteoclast number for A) = 18; B) = 18; C) = 18/12/12/12/12 for 100/500/1000/5000/15000 ng/ml lanthanum respectively; Mean plus or minus SD for A) = 1 plus or minus 0.36; B) 0.15 plus or minus 0.07; C) = 0.70 plus or minus 0.27/0.89 plus or minus 0.29/0.65 plus or minus 0.23/0.05 plus or minus 0.20/0.30 plus or minus 0.19 for 100/500/1000/5000/15000 ng/ml lanthanum respectively.

The above data showed that a clear dose-dependent inhibition was observed with lanthanum (500 - 15000 ng/ml) that was statistically significant from lanthanum (1000 - 15000 ng/ml).

A statistically significant inhibition was also observed with lanthanum (100 ng/ml). In the control group where vitamin D was omitted, osteoclast differentiation was significantly lower than in the baseline

group.

USE - For enhancing bone formation in a mammal (preferably human) having a bone deficit or risk of developing bone deficit or a bone remodeling disorder or is at risk of developing such disorder, e.g. osteoporosis, including primary, secondary, post-menopausal, male or steroid-induced osteoporosis, Paget's disease, osteoarthritis, rheumatoid arthritis, achondroplasia, osteochodrytis, hyperparathyroidism, osteogenesis imperfecta, congenital hypophosphatasia, fibromatous lesions, fibrous displasia, multiple myeloma, abnormal bone turnover, osteolytic bone disease, rickets, osteomalacia and periodontal disease; for treating a human having a bone fracture, bone trauma, or a condition associated with post-traumatic bone surgery, post-prosthetic joint surgery, post-plastic bone surgery, post-dental surgery, bone chemotherapy treatment or bone radiotherapy treatment.

In the preparation of a medicament for treating the above disease and conditions (all claimed).

ADVANTAGE - The lanthanum significantly enhances bone formation in vitro and vivo and also increases bone density in mammals. The lanthanum provides simultaneous actions of stimulating osteoblast differentiation and inhibiting osteoclast differentiation, and also activates bone formation activity of differentiated osteoclasts.

Dwg.0/4

TI Use of **lanthanum** (III) compounds for enhancing bone formation, inhibiting osteoclastic differentiation and/or activating osteoblastic differentiation to treat **bone disease** such as osteoporosis.

AB . . . 20020321

NOVELTY - Enhancing bone formation, inhibiting osteoclastic differentiation and/or activating osteoblastic differentiation to manage, treat or achieve prophylaxis of **bone disease** comprises administering a **lanthanum** compound (preferably **lanthanum** (III)) to a human or animal.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a composition for the **treatment** of a **bone** remodeling disorder comprising the **lanthanum** (III) compound and a bone enhancing agent.

ACTIVITY - Osteopathic; Cytostatic; Antiarthritic; Antirheumatic; Antiinflammatory.

MECHANISM OF ACTION -. . .

TT TT: **LANTHANUM** COMPOUND ENHANCE BONE FORMATION INHIBIT DIFFERENTIAL ACTIVATE DIFFERENTIAL TREAT **BONE DISEASE** OSTEOPOROSIS.

L10 ANSWER 4 OF 4 MEDLINE on STN
AN 2003270795 IN-PROCESS
DN 22638884 PubMed ID: 12753271
TI A multicenter study on the effects of **lanthanum** carbonate (**Fosrenol**) and calcium carbonate on renal **bone disease** in dialysis patients.
AU D'Haese Patrick C; Spasovski Goce B; Sikole Aleksander; Hutchison Alastair; Freemont Tony J; Sulkova Sylvie; Swanepoel Charles; Pejanovic Svetlana; Djukanovic Llubica; Balducci Alessandro; Coen Giorgio; Sulowicz Waldysaw; Ferreira Anibal; Torres Armando; Curic Slobodan; Popovic Milan; Dimkovic Nada; De Broe Marc E
CS Department of Nephrology-Hypertension, University of Antwerp, Belgium.
SO KIDNEY INTERNATIONAL. SUPPLEMENT, (2003 Jun) (85) S73-8. Journal code: 7508622. ISSN: 0098-6577.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030612
Last Updated on STN: 20030612
AB BACKGROUND: Lanthanum carbonate (LC) (Fosrenol) is a novel new treatment

for hyperphosphatemia. In this phase III, open-label study, we compared the effects of LC and calcium carbonate (CC) on the evolution of renal osteodystrophy (ROD) in dialysis patients. METHODS: Ninety-eight patients were randomized to LC (N = 49) or CC (N = 49). Bone biopsies were taken at baseline and after one year of treatment. Acceptable paired biopsies were available for static and dynamic histomorphometry studies in 33 LC and 30 CC patients. Blood samples were taken at regular intervals for biochemical analysis and adverse events were monitored. RESULTS: LC was well tolerated and serum phosphate levels were well controlled in both treatment groups. The incidence of hypercalcemia was lower in the LC group (6% vs. 49% for CC). At baseline, subtypes of ROD were similarly distributed in both groups, with mixed ROD being most common. At one-year follow-up in the LC group, 5 of 7 patients with baseline low bone turnover (either adynamic bone or osteomalacia), and 4 of 5 patients with baseline hyperparathyroidism, had evolved toward a normalization of their bone turnover. Only one lanthanum-treated patient evolved toward adynamic bone compared with 6 patients in the CC group. In the LC group, the number of patients having either adynamic bone, osteomalacia, or hyperpara decreased overall from 12 (36%) at baseline to 6 (18%), while in the calcium group, the number of patients with these types of ROD increased from 13 (43%) to 16 (53%). CONCLUSION: LC is a poorly absorbed, well-tolerated, and efficient phosphate binder. LC-treated dialysis patients show almost no evolution toward low bone turnover over one year (unlike CC-treated patients), nor do they experience any aluminum-like effects on bone.

TI A multicenter study on the effects of **lanthanum** carbonate (**Fosrenol**) and calcium carbonate on renal **bone disease** in dialysis patients.